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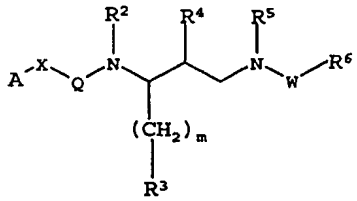
10 February 2000 (10.02.00)

(54) Title: MULTI-DRUG RESISTANT RETROVIRAL PROTEASE INHIBITORS AND USE THEREOF



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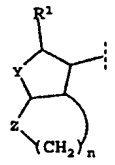

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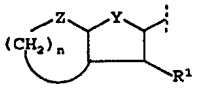

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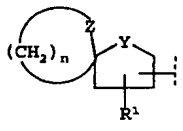

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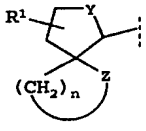

(V)

(57) Abstract

The present invention generally provides a retroviral protease–inhibiting compound represented by formula (I), or a pharmaceutically acceptable salt, a prodrug, or an ester thereof, wherein A is a group of formula (II), (III), (IV), or (V); R^1, R^2, R^3, R^5, or R^6 is H, or an optionally substituted and/or heteroatom–bearing alkyl, alkenyl, alkynyl, or cyclic group; Y and/or Z are CH_2, O, S, SO, SO_2, amino, amides, carbamates, ureas or thiocarbonyl derivatives thereof, optionally substituted with an alkyl, alkenyl, or alkynyl group; n is from 1 to 5; X is a bond, an optionally substituted methylene or ethylene, an amino, O or S; Q is C(O), C(S), or SO_2; m is from 0 to 6; R^4 is OH, =O (keto), NH_2, or alkylamino, including esters, amides, and salts thereof; and W is C(O), C(S), S(O), or SO_2; wherein the compound inhibits a multidrug–resistant retroviral protease. Optionally, R^5 and R^6, together the N–W bond of formula (I), comprise a 12– to 18–membered ring. Also provided are pharmaceutical compositions for, and therapeutic methods of, treating a multidrug–resistant retroviral infection in a mammal.

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INTERNATIONAL SEARCH REPORT

Inte onal Application No
PCT/US 99/14120

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 C07D493/04 C07D491/04 C07D495/04 A61K31/34

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 C07D

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 97 19055 A (NOVARTIS AG) 29 May 1997 (1997-05-29) page 1 -page 14 ---	1,14
A	WO 96 28463 A (G. D. DEARLE & CO.) 19 September 1996 (1996-09-19) page 4 -page 14, line 12 page 145 -page 189 ---	1,14
A	WO 95 06030 A (G. D. SEARLE & CO.) 2 March 1995 (1995-03-02) page 4 -page 18, paragraph 21 page 192 -page 212 ---	1,14
A	WO 94 14793 A (G. D. SEARLE & CO.) 7 July 1994 (1994-07-07) page 3, line 10 -page 13 --- -/--	1,14

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

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Date of the actual completion of the international search	Date of mailing of the international search report
14 December 1999	21/12/1999

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31–70) 340–2040, Tx. 31 651 epo nl, Fax: (+31–70) 340–3016	Kyriakakou, G

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
A	US 5 753 660 A (JAMES A. SIKORSKI ET AL.) 19 May 1998 (1998-05-19) the whole document	1,14
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INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 99/ 14120

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.: 17-21
because they relate to subject matter not required to be searched by this Authority, namely:
Remark: Although claims 17-21 is are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

2. [ ] Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application. as follows:

1. [ ] As all required additional search fees were timely paid by the applicant. this International Search Report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fee. this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant. this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

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